

6 AGA GGG AATTGGCACGAGGCAGCATGGAGCCTCGGCTGACTGGCTGGCC  
 .GA GAA CAG? NT 216.20 1  
 EX 12 EX 13 EX 14  
 ACGGCCGCGGCCGGGTGGGTAGAGGAGGTGGCGGGCGCTGCTG  
 EX 13 NT 216.3  
 GAGGCGGTGGCGCTGCCAACGCACCGAACAGTTACCGTGGAG  
 EX 12 EX 13 EX 14  
 GCCGATCCAGG CATGATGATGGCAGCGCCCCGAGTGGCGGAG  
 EX 12 EX 13 EX 14  
 CTGCTGCTGCTCCACGGCGGGAGCCAACTGCCCGACCCGCCA  
 216 INT EX 12 EX 13 EX 14  
 CTCTCACCCGACCCGTGCACGACCGCTGCCGGAGGGCTCTGGAC  
 NT 216.5 EX 12 EX 13 EX 14  
 ACGCTGGTGGTGCTGCACCGGGCCGGCGCGCTGGACGTGCGC  
 EX 3  
 GATGCCTGGGCCGTGCTGCCGTGGACCTGGCTGAGGAGCTGGC  
 EX 12 EX 13 EX 14  
 CATCGCGATGTCGCACGGTACCTGGCGCGGCTGCGGGGGCACC  
 EX 12 EX 13 EX 14  
 AGAGGAGTAACCATGCCCGATAGATGCCCGGAAGGTCCCTC  
 EX 8 EX 12 EX 13 EX 14  
 AGACATCCCCGATTGAAAGAACAGAGAGAGGCTCTGAGAAACCTC  
 EX 5 EX 12 EX 13 EX 14  
 GGGAAACTTAGATCATCAGTCACCGAACGGCTCTGAGAAACCTC  
 ACTGCCCGCCACAACCCACCCGCTTCGTAGTTTCAATTAGA  
 AAATAGAGCTTTAAAAATGTCCTGCCTTTAACGTAGATATAA  
 GCCTCCCCCACTACCGTAAATGTCCATTATATCATTTTATAT

Figure 1A

ATTCTTATAAAAATGTAAAAAAGAAAAACACCGCTCTGCCTTT  
TCACTGTGTTGGAGTTCTGGAGTGAGCACTCACGCCCTAAGCG  
CACATTCATGTGGGCATTCTTGCAGCCTCGCAGCCTCCGGAAG  
CTGTCGACTTCATGACAAGCATTGTGAAGTAGGAAAGCTCAG  
GGGGGTTACTGGCTCTCTGAGTCACACTGCTAGCAAATGGCAG  
AACCAAAGCTCAAATAAAAATAAAATTATTCATTCACT  
CAAAAAAA

Figure 1B

Figure 2A

p16EX1 < GGNNGNAAGNTGTGGGGAAAGTTGGGATGGAANACCAANCCCTCCTTCNTTACCAA 60  
 .....+.....+.....+.....+.....+.....+.....+  
 p16EX1 < ACNCTGGCTCTGNCGAGGCTNCNTCCGANTGGTNCCCCGGGGAGACCCAACCTGGNC 120  
 .....+.....+.....+.....+.....+.....+  
 p16EX1 < GACTTCAGGGNTGCNACATTCACTAAGTGTNGGAGNTAATANCACCTCCGAGCANx 180  
 p16EX13 < TCNCTTATTGNTAGGANATAATAACACCTCCACCCGATAACT 41  
 .....+.....+.....+.....+.....+.....+  
 p16EX1 < TCGCTCACAGCGTCCCCTTACCTNGANAGATACCNCNxGxTCCCTCCAGAGGATTGAGG 240  
 p16EX13 < TcaCTTACAACGTCCCNNTtCCTGgaAAGATAcacaGCCTCCAGAGGATTGTGG 101  
 .....+.....+.....+.....+.....+  
 p16EX1 < GACAGGNTCGGAGGGGGCTCTCCCCCANCACCGGAGGAAGAAAGAGGAGGGNCTGACTG 300  
 p16EX13 < GACAGGGTNGGAGNGGTCTCTCCNCCACCACCGGAGGAAGAAAGAGGAGGGCTGNCTG 161  
 .....+.....+.....+.....+.....+.....+.....+  
 p16EX1 < GTCACCAGAGGGTGGGACGGACCGCGTGCCTCGCGNCTNCGGAGAGGGGAGAACAGA 360  
 p16EX13 < TTCACCAGAGGGTGGGACGGACCGACNCGTACGCTCGNCGNCTNCGGAGAGGGGAGAGCACT 221  
 .....+.....+.....+.....+.....+.....+  
 p16EX1 < CAACGGGGCCGGGGAGCAGCATGGATCCGGCGGGAGCAGCATGGANCCTCGACT 420  
 p16EX13 < CANCGNCGNCGGGAGCAACATGGAACCGNCGGGAGCAGCATGGANCCTCGGCT 281  
 .....+.....+.....+.....+.....+  
 P16NT2 ? < GACNNNCTCCGGCCGGNGTCGGTAGAGGGAGGTGCAGGGCGCTGCTGGAG 49  
 p16EX1 < GACTGACTGCCTCGC 435  
 p16EX13 < GACTGGCTGNCCACGNCCACGNCCCAGGTAGAGGGAGGTGCAGGGCGCTNCTGGAG 341  
 .....+.....+.....+.....+.....+  
 P16NT3 > E + 13 STGTNANCCCGGGTA 15  
 P16NT2 < GCGGGGGCGCTGCCAACGCAACGAATAGTTACGGTCGGAGGCCGATCAGGTxxGGGTA 109  
 p16EX13 < GCGGGGNCTCTGNCCAACNCGCTAAAAN 369  
 .....+.....+.....+.....+.....+  
 P16NT3 > GAGGGTCTGCAGCGGGAGCAGNGGATGGCGGGCGACTCTGGAGGACGAAGTTGCAGGG 75  
 P16NT2 < GAGGGTCTGCAGCGGGAGCAGGGATGGCGGGCGACTCTGGAGGACGAAGTTGCAGGG 169  
 .....+.....+.....+.....+.....+  
 P16NT3 > AATTGGAATCAGGTAGCGCTTCGANTCTCCGGAAAAAGGGGAGGCTTCTGGGGAGTTNN 135  
 P16NT2 < AATTGGAATCAGGTAGCGCTTCGATTCTCCNGAAAAAGGGGAGGCTTCTGGGGAGTTTT 229

Figure 2B

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Figure 2C

16INT > AAAANNAAAAAAATCTCCCAGGCCTAACATAATTNTCAGGAAAGAAATTCAGTAGTTG 60  
.....+.....+.....+.....+.....+.....+.....+  
16INT > NATCTCAGGGAAATACAGGAAGTTAGCCTGGAGTAAAAGTCAGTCTGTCCTGCCCTGCCCTT 120  
.....+.....+.....+.....+.....+.....+.....+  
6INT > TGCTANATTGCCCGTGCCTCACAGTGCTCTGCCTGTGACGACAGCTCCNCAGAAGTTC 180  
.....+.....+.....+.....+.....+.....+.....+  
6INT > GGAGGATATAATGGAATTCAATTGTACTGAAGAATGGATAGAGAACTCAAGAAGGAAAT 240  
.....+.....+.....+.....+.....+.....+.....+  
6INT > TGGAAACTGGAAGCAAATGTAGGGTAATTAGACACCTGGGCTTGTGTTGGGGCTGCT 300  
6EX15 < AANAAAAaAgAAATNgAtAANATagAGGAat 31  
.....+.....+.....+.....+.....+.....+.....+  
6INT > TGGCGGTGAGGGGGCTCTACACAAGCTTCCCTTCCGTATGCCGNCCCCACCCGGCTC 360  
6EX15 < ~~GA~~ANATTAAAAT~~AAA~~AGANAGANAGA~~ta~~AtAAAAAAACGag~~AT~~gTT~~t~~AGAG 91  
.....+.....+.....+.....+.....+.....+.....+  
6INT > TGACCATTCCTGTTCTCTGGCAGGT<sup>I</sup>CATGATGATGGGCAGCGCCCGACTGGCGGAGCTG 420  
6EX15 < NTAAT~~ta~~ATTATA~~aa~~g~~te~~AAg~~AG~~CTGATGATAT~~AA~~AGGA~~aa~~At~~tg~~AGGGAA~~tt~~ta 151  
.....+.....+.....+.....+.....+.....+.....+  
6INT > CTGCTGCTCCACGGCGGGAGCCAACTGCTCCGACGCCG 460  
6EX2 > CCTGCNACGACCCCGCCACTCTCACCCGACCCGTG 35  
6EX14 > NCTCTCACGGTGGGGAGGCCAACTGCGCCGAACCCGCCACTCTCACCCGACCCGCG 56  
6EX15 < act~~Ag~~ACAANNGNAT~~AA~~ANAAATT~~CC~~ACACCCGCCACTCTCACCCGATCCGTG 211  
.....+.....+.....+.....+.....+.....+.....+  
6EX2 > CACGACGCTGTCCGGGAGGGTTCTGGACACGCTGGTGGTGTGCACCGGGCCGGGNG 95  
6EX14 > CACGACGGTGCCCCGGGAGGGTTCTGGACACGCTGGTGGTGTGCACCGGGCCGGGNG 116  
6EX15 < CTCGACACTGCCCGGGAGGT~~CT~~NTCC~~CT~~GGACACGCTGGTGGTNCTCCACCGNCCGGGCA 271  
.....+.....+.....+.....+.....+.....+.....+  
EX2 > CGGTTGGACGTGCGCGATGCCTGGGGCCGCNTCCGTGG~~x~~ACCTGGTTGAGGAGCTGGG 155  
EX14 > CGGCTGGACGTTCGNGATGCCTGGGGC~~NT~~CTNTCCGTNG~~x~~ACCTGGCTGAAGAGCTGGN 176  
EX15 < CGTCTGGACGTGCGCGATGCCTGGGNCCGNCTACCCGTGGTACCTGACTGAGGACCTGGG 331  
.....+.....+.....+.....+.....+.....+.....+  
EX2 > NCATCGCGATGTGCGCACGGTACCTGGCGCGTTGC~~GGGGGG~~ACCA~~GAGG~~~~x~~NAGTNACC 215  
EX14 > NCATCGNGATGTGCGCACGGCNCTGTGTGNGNTGC~~GGGGGG~~ACCA~~TAGG~~TCAGTNCC 236  
EX15 < CCATCCC~~GAT~~TTGCGNGGGTANCTGNGNGGCTGN~~GGGG~~CCAANAGAGG~~x~~CANTACCC 391

Figure 3A

>16EX5 < xAAGTATGAGCGAACNAATTGTGGTTGAGAANAGGNAATCGTAGGAACTTCGGGATC 60  
 .....+.....+.....+.....+.....+.....+  
 >16EX5 < CCNCNGGANCNCCAGAACCTGAGNCGCCATTGAAATNACAAACTGNCTGNATCACTC 120  
 .....+.....+.....+.....+.....+.....+  
 >16EX5 < CGNACCAGGTNCAAAAGATACTGGGANGCGGAAGGGAAAGACNACATCNAGACCGCC 180  
 >16EX9 < CCCC 4  
 .....+.....+.....+.....+.....+.....+  
 >16EX5 < TTGCGNCCTXGGNATTGTGAGCAGCCTCTGAGACTCATTXATATNACACTCGTXXTTCTT 240  
 < ATCGCGCCTTGGGANTGTGAGCNACCATTGAGACTCATNAATATAGCACTCGTTTCTT 64  
 .....+.....+.....+.....+.....+.....+  
 >16EX5 < CTTACAAACCTGCGGNCCGCGCGGTGCGCCTTCTCTGCCCTCCGCCGGTGGACCTGG 300  
 >16EX9 < CTTGCAACCCCTGCGGNCCGCGCGGTGCGCCTNTCTCTGCCCTCCGCCNGGTGGACCTGG 124  
 .....+.....+.....+.....+.....+.....+  
 >16EX5 < GCGCTTGAGCGGTGGCGCCCTGGAGCAGCCAGGCAGNCAGTGGACTAGCTGCTGGACC 360  
 >16EX9 < GCGCTTGAGCGGTGGCGCCNCCTGGANCAGCCAGGCAGGCAGTGGACTACCTNCTGGACC 184  
 .....+.....+.....+.....+.....+.....+  
 >16EX5 < AGGGAGGTGTGGGAGAGCGGTGGCGGCCGGTACATGCACGTGAAGCCATTGCGAGAACTT 420  
 >16EX9 < AGGGAGGTGTGGGAGAGCGGTGNCGGCGGGTACATGCACGTGAAGCCATTGCGAGAACTT 244  
 .....+.....+.....+.....+.....+.....+  
 >16EX5 < TATCCATAAGTATTCAATACCGTAGGGACGGCAAGAGAGGGAGGGCGGGATGTGCCACA 480  
 >16EX9 < TATCCATAAGTATTCAATGCCGTAGGGACGGCAAGAGAGGGAGGGCGGGATGTNCCACA 304  
 .....+.....+.....+.....+.....+.....+  
 >16EX5 < CATCTTGACCTCAGGTTCTAACGCCTGTTCTGCCCTCTGCAGACAACCCCGA 540  
 >16EX9 < CATCTTGACCTCAGGTTCTAACGCCTGTTCTGCCCTCTGCAGACATCCCCGA 364  
 .....+.....+.....+.....+.....+.....+  
 >16EX4 > AGAAATTAGATCATCAGTCACCGATG 26  
 >16EX5 < TTGAAAGAACCAAGAGAGGCTCTGAGAAC 570  
 >16EX9 < TTGAAAGAACCAAGAGAGGCTCTGAGAACCTCCGGAAACTTAGTCATCACTGCCGNA 424  
 .....+.....+.....+.....+.....+.....+  
 >16EX4 > GTCCTACAGGGNCACAACTGNCCCCGCCACAACCCACCCCGNTTCGTAGTTTCAATT 86  
 >16EX9 < AA 426  
 .....+.....+.....+.....+.....+.....+

Figure 3B

p16EX4 > GAAAATAGAGCTTTAAAAATGTCCTGCCTTTAACGTAGATATATGCCTCCCCCACTA 146  
 .....+.....+.....+.....+.....+.....+  
 p16EX4 > CCGNAAATGTCCATTTATATCATNTTTATATATTCTTATAAAAATGTAAGAAAAAGAAAAA 206  
 .....+.....+.....+.....+.....+.....+  
 p16EX4 > CACCGCTTCTGCCTTTCACTGTGTTGGAGTTCTGGAGTGAGCACTCACGCCCTAACG 266  
 .....+.....+.....+.....+.....+.....+  
 p16EX6 > CANCNATNTNCGGCATTCTNGNGAGCCTCGTAGTCTCCGGATGNTGTCGACCTCGAG 58  
 p16EX6a > CANCNATNTNCGGCATTCTNGNGAGCCTCGTAGTCTCCGGATGNTGTCGACCTCGAG 58  
 p16EX4 > GCACATTCACTGTGGGCATTTCTTGCAGCCTCGCAGNCTCCGGAAGCTGTCGACCTCGAG 326  
 .....+.....+.....+.....+.....+.....+  
 p16EX6 > GGGGGGNCCNGTACCCAATTGNCCTATNGTAGTCGTNTTACAATTCACTGGCCGCCGT 118  
 p16EX6a > GGGGGGNCCNGTACCCAATTGNCCTATNGTAGTCGTNTTACAATTCACTGGCCGCCGT 118  
 p16EX4 > GGGGGGNCCGGTACCCAATTGCCCTATAGTAGTCGTATTACAATTCACTGGNCNGN 386  
 .....+.....+.....+.....+.....+.....+  
 p16EX6 > TTTxACAACGTCGxTGxACTGGAAAACCCCTGGTGTACCCAACTTxATCGCCTTGNAG 178  
 p16EX6a > TTTxACAACGTCGxTGxACTGGAAAACCCCTGGTGTACCCAACTTxATCGCCTTGNAG 178  
 p16EX4 > TTTTACAACGTCGGTGGACTGGAAAACCCCGGNGTTACCCAACTTAATCGNCTGGAG 446  
 .....+.....+.....+.....+.....+.....+  
 p16EX6 > NACATCCCCCTTxCGCCAGCTGGTGTAAATAGCGANGAGGCCGCACCGATCGCCCTTCC 238  
 p16EX6a > NACATCCCCCTTxCGCCAGCTGGTGTAAATAGCGANGAGGCCGCACCGATCGCCCTTCC 238  
 p16EX4 > GACATCCCCTTTCGCCAGNTGGGTTATAGNGAAGAGGGCCNCACCNNTGCC 502  
 .....+.....+.....+.....+.....+.....+  
 p16EX6 > CAACAGTTGNGCAGCCTGAATGGCGAATGGAATTGTAAGCGTTAATATTTGTTAAAAT 298  
 p16EX6a > CAACAGTTGNGCAGCCTGAATGGCGAATGGAATTGTAAGCGTTAATATTTGTTAAAAT 298  
 .....+.....+.....+.....+.....+.....+  
 p16EX6 > TCGCGTTANATCNCGGTTAANTCAGCTCATNTTTATCCAATAGGCCGANATCGGCANA 358  
 p16EX6a > TCGCGTTANATCNCGGTTAANTCAGCTCATNTTTATCCAATAGGCCGANATCGGCANA 358  
 .....+.....+.....+.....+.....+.....+  
 p16EX6 > ATCCCCAATAAATCAANAGAATAGACCGAGATAGGGTTGAGTGTGTTCCAGTTNGGAA 418  
 p16EX6a > ATCCCCAATAAATCAANAGAATAGACCGAGATAGGGTTGAGTGTGTTCCAGTTNGGAA 418  
 .....+.....+.....+.....+.....+.....+  
 p16EX6 > CANGAGTCCACTATTAAAGANCCTAGNCTCNAACGTCAAGGGCGAAAAACCNNTTCA 478  
 p16EX6a > CANGAGTCCACTATTAAAGANCCTAGNCTCNAACGTCAAGGGCGAAAAACCNNTTCA 478  
 .....+.....+.....+.....+.....+.....+  
 p16EX6 > GNNGATTGGNCCACTACGCNTANCC 503

# Figure 3C

16EX6a > GNGGATTGGNCCACTACGCNTANCCATCACCTATTG 515  
.....+.....+.....+.....+.....+.....+

Figure 4

Figure 5

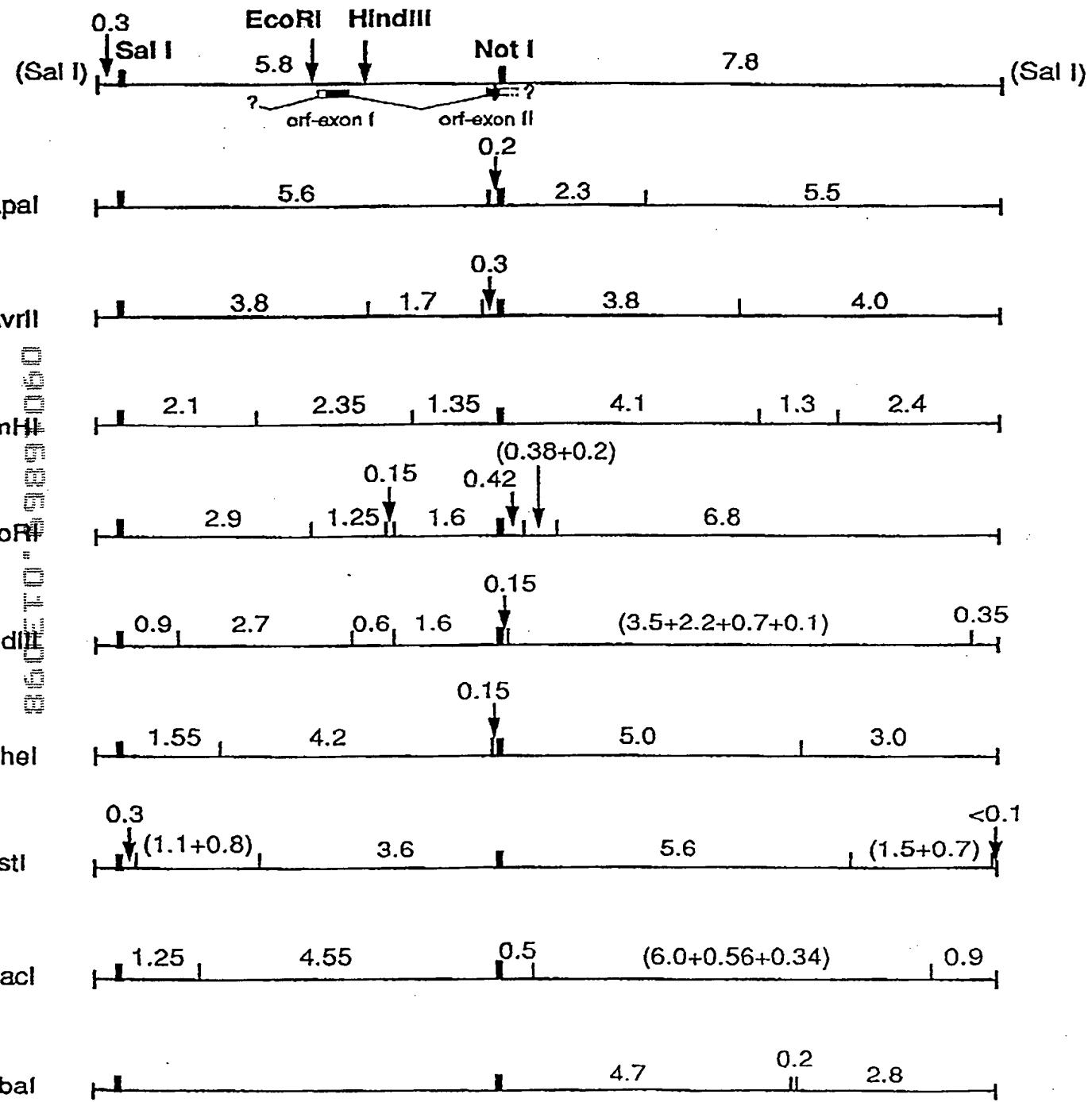


Figure 6

p16: Ile Gln Val Met Met Met Gly Ser Ala Arg Val Ala Glu Leu Leu Leu His Gly Ala Glu Pro Asn Cys Ala Asp Pro Ala  
p15: Ile Gln Val Met Met Met Met Gly Ser Ala Arg Val Ala Glu Leu Leu Leu His Gly Ala Glu Pro Asn Cys Ala Asp Pro Ala  
p13: Met Met Met Gly Asn Val His Val Ala Leu Leu Leu Asn Tyr Gly Ala Asp Ser Asn Cys Glu Asp Pro \*

Thr Leu \* Thr Arg Pro Val His Asp Ala Ala Arg Glu Gly Phe Leu Asp Thr Leu Val Val Leu His Arg Ala Gly Ala Arg  
Thr Leu \* Thr Arg Pro Val His Asp Ala Ala Arg Glu Gly Phe Leu Asp Thr Leu Val Val Leu His Arg Ala Gly Ala Arg  
Thr Thr Phe Ser Arg Pro Val His Asp Ala Ala Arg Glu Gly Phe Leu Asp Thr Leu Val Val Leu His Gly Ser Gly Ala Arg

Leu Asp Val Arg Asp Ala Trp Gly Arg Leu Pro Val Asp Leu Ala Glu Leu Gly His Arg Asp Val Ala Arg Tyr Leu Arg  
Leu Asp Val Arg Asp Ala Trp Gly Arg Leu Pro Val Asp Leu Ala Glu Glu Arg Gly His Arg Asp Val Ala Gly Tyr Leu Arg  
Leu Asp Val Arg Asp Ala Trp Gly Arg Leu Pro Leu Asp Leu Ala Gln Glu Arg Gly His Gln Asp Ile Val Arg Tyr Leu Arg

Ala Ala Ala Gly Gly Thr ....  
Thr Ala Thr Gly Asp  
Ser Ala \* Gly Cys Ser ....